REMARKS

Applicants acknowledge denial of priority to the applications set forth in the deleted paragraph and accept the priority of the present filing date which is 6 July 2000. The sequence of the nucleic acids encoding the T-type α_{1G} subunit were first disclosed in this application. The originally filed claim to benefit of earlier applications is now specifically disclaimed.

Applicants appreciate the withdrawal of the previous rejections.

Only one basis for rejection remains - asserted lack of utility for the claimed DNA molecules and associated recombinant materials and methods.

Prior to presenting evidence in support of applicants' position that these materials satisfy the requirements of the statute, applicants wish to make the following preliminary observations:

1. The present specification lists, as "conditions where undesirable T-type calcium channel activity is present" the following: epilepsy, sleep disorders, mood disorders, cardiac hypertrophy and arrhythmia, hypertension (page 5, lines 15-17) and, in addition, hormone secretion and fertilization (page 9, lines 26-27) as well as migraine ataxia, schizophrenia, angina, depression and Parkinson's disease (page 9, lines 19-20).

2. Applicants need only show evidence that supports the nexus between T-type channel misbehavior and one of these conditions, not all. A summary of this principle is found in Chism on Patents, section 4.04(4). Chism quotes *Raytheon Co. v. Roper Corp.*, 724 F2d 951, 220 USPQ 592 (Fed. Cir. 1983): "When a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown". Chisum also quotes *Standard Oil Company v. Mount Edison SPA*, 664 F2d 356, 212 USPQ 327 (3rd Cir. 1981): "Proof of one of the disclosed utilities suffices to meet the statutory utility requirement."

It is within the authority of the Office to allow claims when only one utility is shown, but to require removal of reference to other listed utilities that are "incredible or misleading." However, this standard is fairly high, it appears, as noted in *In re Hozumi*, 226 USPQ 353 (Commissioner of Pat. and Trademarks 1985) where it was held appropriate for the Office to require removal of "wildly speculative statements." Further, "the cancellation of speculative statements does not in any way affect the scope of protection provided by the claimed subject matter in this or any other application."

Thus, for purposes of finding the claims allowable, a nexus between only one of the listed indications and T-type channels need be shown.

3. Reference in the previous response to there being no claims to "compounds" was in the context where "compounds" was meant to denote compounds identified as therapeutics by using the claimed recombinant materials (which materials are also, of course, compounds) as screening tools. This distinction is relevant because, as noted in MPEP § 2701.01 1(b) on page 2100-33 of the August 2005 edition,

> Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations in other cases to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement (cited *Brenner v. Manson*) rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility.

This is the case here, where compounds not yet identified using the tools of the invention may not be currently available, but they can certainly be identified using the tools of the invention and their utility once they are identified has been specified.

4. While the Office, using its own method, apparently failed to find any documents with a nexus between T-type calcium channel and schizophrenia or Parkinson's disease in a PubMed™ search, there is already evidence before the Office that such a nexus was known in the art. In a previous Office action mailed 21 December 2004, the Office rejected the claims as assertedly anticipated by Dubin, *et al.,* U.S. patent 6,358,706 ('706). As acknowledged prior art, the disclosure of Dubin, *et al.,* may be reviewed for what it says about the physiological role of T-type calcium channels. The '706 patent is also directed to an α_{1G} T-type calcium channel subunit which has a slightly different structure from that claimed herein. Thus, the activities reported for this α_{1G} subunit should be the same as those appropriate here. Column 6, beginning at line 37, lists the conditions that are mediated by this activity as

> ...epilepsy, schizophrenia, depression, sleep disorders, stress, endocrine disorders, respiratory disorder, peripheral muscle disorders, muscle excitability, Cushing's disease, fertilization, contraception, disorders involving neuronal firing regulation, respiratory disorders, hypertension, cardiac rhythm, potentiation of synaptic signals, improving arterial compliance in systolic hypertension, vascular tone such as by decreasing vascular swelling, cellular growth (protein synthesis, cell differentiation and proliferation), cardiac hypertrophy, cardiac fibrosis, atherosclerosis, cardiovascular disorders including, but not limited to: myocardial infarct, cardiac arrhythmia, heart failure, and angina pectoris.

In light of the power, indeed responsibility, of the Office to remove "incredible or misleading" utilities from issued patents, the inclusion of these indications in the '706 patent is especially significant.

5. There is no doubt that the claimed sequence represents a T-type calcium channel. This is demonstrated in the specification in Example 3 on pages 21-23. The claimed nucleic acid

molecule indeed "encodes a calcium channel with typical properties of a T-type current." (Page 23, lines 13-14.)

6. Summary: there is no doubt that the claimed recombinant materials are those which generate a T-type calcium channel since a working example shows this. There is no doubt raised that it would be possible to use such materials to screen compounds in order to identify those which agonize or antagonize calcium ion activity in T-type channels. A credible nexus between T-type channel misbehavior and only one disease condition need be shown. Evidence is already of record, and cited by the Office that a nexus exists between T-type channel misbehavior and a litany of diseases, including those listed by applicants.

The Guidelines provided by the Office with regard to utility provide that the utility must be specific, substantial, and credible. There can be no issue that the utility asserted by applicants is substantial and specific. Applicants have asserted that the compounds that are identified by screens using the recombinant materials of the invention would have specific uses in treating specific conditions. The conditions referred to are specific to the T-type calcium channel, not just any calcium channel, and not just any biological molecule that could be encoded by any recombinant materials. And how could it be that the ability to treat the conditions listed is not substantial? What appears to be at issue is "credibility" – *i.e.*, the Office appears to assert that the nexus asserted by applicants with respect to the specific and substantial uses is not credible. As the Office is aware, it has the initial burden to provide a *prima facie* showing as to why the utilities claimed are to credible.

Respectfully, applicants believe no *prima facie* case has been made.

Nevertheless, the following prior art documents clearly demonstrate that the skilled practitioner recognizes a nexus between the conditions described and the necessity to provide materials that interact with T-type channels.

For example, U.S. patent 6,309,858 which has a § 102(e) date at least as early as 23 September 1999, describes the nexus between T-type channels and peripheral pain (column 2, lines 6-13).

Arnoult, C., *et al., PNAS* (1996) 93: 13004-13009 describe the involvement of T-type calcium ion channels in sperm as linked to fertilization (see abstract).

Tsakiridou, E., *et al., J. Neurosci.* (1995) 15:3110-3117 demonstrate the involvement of T-type calcium channels in epilepsy.

Coulter, D. A, *et al., Br. J. Pharmacol.* (1990) 100:800-806 further showed the nexus between T-type channels and epilepsy.

Rossier, M. F., *et al., Endocrinol.* (1996) 137:4817-4826 demonstrate the nexus between T cell activity and aldosterone genesis. On page 4826, these authors indicate that this nexus is relevant in the treatment of hypertension.

Enyeart, J. J., *et al., Mol. Pharmacol.* (1992) 42:364-372 shows the nexus of the T-type channels with schizophrenia (see page 371, third full paragraph) as well as with epilepsy and arrhythmia (same page, fifth paragraph). This document further discloses a drug that blocks T-type calcium channels (ethosuximide) is useful in the treatment of absence seizures (epilepsy).

These are but a few of many documents that link T-type malfunction with serious conditions that require treatment. Thus, there can be little doubt, that the ordinary practitioner would recognize

that the recombinant materials as useful screening tools where the purpose of the screen is well defined, specific, substantive and credible.

As the asserted lack of utility was also the basis for rejection under 35 U.S.C. § 112, paragraph 1, it is believed that the foregoing is responsive to this ground of rejection as well. Accordingly, withdrawal of the rejection is respectfully requested. Passage of pending claims 1-2, 4-6, 14 and 18-26 to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 381092000721.

Respectfully submitted,

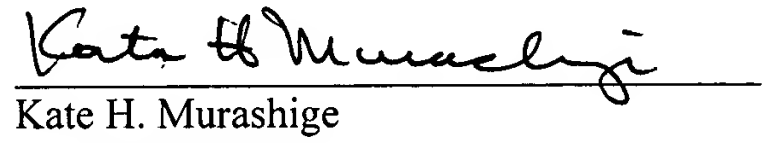
Dated: January 4, 2006 By: 

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EXHIBIT

U.S. patent 6,309,858.

Arnoult, C., *et al. PNAS* (1996) 93: 13004-13009.

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